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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,581	08/19/2003	Laurie H. Glimcher	HUI-041DV	3956

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LAHIVE & COCKFIELD, LLP
ONE POST OFFICE SQUARE
BOSTON, MA 02109-2127

EXAMINER

LI, QIAN JANICE

ART UNIT	PAPER NUMBER
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1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/643,581	Applicant(s) GLIMCHER ET AL.	
	Examiner Q. Janice Li, M.D.	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4 and 14-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4 and 14-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment and remarks filed 1/25/07 are acknowledged. Claims 1, 2, 4 have been amended, claims 3, 5-13 have been canceled. Claims 14-23 are newly submitted. Claims 1, 2, 4, 14-23 are pending in the application and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims, and persuasive argument will not be reiterated. The arguments in 1/25/07 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 14-23 stand rejected or are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using XBP-1 knockout mouse *embryo*, or *chimeric* mice that is XBP-1 deficient/RAG-2 deficient, does not reasonably provide enablement for making and using XBP-1 knockout mice or XBP-1 conditional knockout mice. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

Art Unit: 1633

connected, to practice the invention commensurate in scope with these claims, for reasons of record and following.

As an initial matter, it is noted applicants amended claim 1 to recite stimulates in place of “modulates” in the preamble and line 8, however, “a modulator” in line 7 has not been amended to be consistent with the other amendments.

As to the recited XBP-1 deficient mice, the amendment had made it clear that they encompass XBP-1 knockout or conditional knockout mice. In view of the specification, the only XBP-1 deficient hepatocytes taught in the specification were obtained from the XBP-1 gene knockout (XBP-1^{-/-}) *embryos* because XBP-1 gene knockout is lethal and the embryo would die *in utero*, and cannot survive to mature (e.g. example 1). Apparently, the mature XBP-1^{-/-} ko mice as claimed cannot be made. Example 2 of the specification teaches making XBP-1^{-/-} /RAG-2^{-/-} chimeric mice by injecting mouse XBP-1^{-/-} ES cells to RAG-2 blastocyst, and through a mechanism called RAG-2-deficient blastocyst complementation. The specification teaches XBP-1 deficient ES cells contribute to about half the mice born, primarily in peripheral B- and T-lymphocytes, and variably to heart, lung, kidney, and muscles, minimally affects liver cells, and thus the specification does not support the full scope of the claims.

As to the conditional knockout mouse in claim 22, the specification as filed contemplates using a tet-regulatory system for conditional disruption of a gene, and referring to methods as disclosed in prior art patents (Specification, page 55). However, the cited patent teaches use of the construct in cultivated cells, but not

Art Unit: 1633

the predictability or lack thereof using the construct for making transgenic animals, or how to regulating the construct in a transgenic animal, or the phenotype of such conditional XBP-1 knockout mice. Moreover, as taught in the specification, the XBP-1 deficiency influences the early development of hepatocyte, differentiation of plasma progenitor B cells, the specification is completely silent with regard to the whether the conditional construct could sufficiently turn on/off the XBP-1 gene and leads to clinically detectable phenotype changes, and thus the disclosure fails to support the full scope of the claims.

Claims 17-19 recite "B cell activity", however, the only B cell activity taught in the specification, influenced by the XBP-1 deficiency is the ability to differentiate to plasma cells. Hence, the specification fails to support the full scope of the claims.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite the limitation "B cell activity". There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

Claim 21 is objected to because of the word "IL1-5". Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 28 of U.S. Patent Application No. 10/655,620, for reasons of record.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It is noted multiple applications filed by applicant are co-pending. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant

Art Unit: 1633

contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Art Unit: 1633

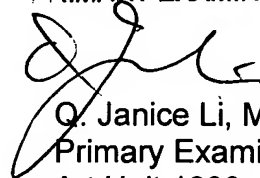
Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER



Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
April 12, 2007